Le syndrome du chromosome 20 en anneau : étude électro clinique à propos d'un cas

Ring chromosome 20 syndrome: Electroclinical description about one case

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RÉSUMÉ

Introduction : Le syndrome du chromosome 20 en anneau est caractérisé par l'association d'une épilepsie, déficience intellectuelle et une dysmorphie faciale. L'EEG semble un examen clé surtout en présence d'un tableau atypique.

Observation : nous rapportons le cas d'une fille âgé de 2 ans qui nous a été adressée pour épilepsie. L'examen clinique a objectivé une dysmorphie faciale, une microcéphalie et un retard psychomoteur. Son EEG inter critique a montré des ondes lentes de grande amplitude dans les régions frontales suggestives du diagnostic de chromosome 20 en anneau qui a été confirmé par le caryotype. Elle a été mise sous antiépileptique mais la patiente continue à faire ses crises.

Conclusion : L'EEG est un examen clé dans le syndrome du chromosome 20 en anneau.

ABSTRACT

Introduction : Ring chromosome 20 syndrome is a rare chromosomal disorder characterized by refractory electroclinical epilepsy syndrome, mild to moderate mental retardation, behavioural disturbances.

Case report : a 2-year-old girl was referred to our department for epilepsy. Her clinical examination showed microcephaly, psychomotor development delay and facial dysmorphia. The inter-ictal EEG showed a bifrontal theta-delta activity suggesting a ring chromosome 20 syndrome. The patient was treated by acid valproic without success than levetiracetam and clonazepam witch reduced the frequency of the seizures.

Conclusion : The ring chromosome 20 syndrome is characterized by mental disability, behavioral disturbances and epilepsy. Ictal EEG may be helpful for the diagnosis.

Mots clés : enfant ; Chromosome 20 en anneau ; Épilepsie

Keywords : child; ring 20 syndrome; epilepsy

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INTRODUCTION :

Ring chromosome (r(20)) is a rare chromosomal disorder that occurs in about 1/30,000 to 1/60,000 living births(1). This syndrome is reported to be one of the most frequent subtypes of the ring chromosome syndromes(1).
R (20) is characterized by refractory epilepsy, with seizures in wakefulness and sleep, behavioral problems and mild to severe cognitive impairment. Facial dysmorphism or other congenital malformations are rarely reported making it difficult to diagnose the syndrome based on clinical findings alone.
The aim of the current study was to analyze the electroclinical data of a r(20) syndrome patient and compare these with the available literature. We focused on the presenting epileptic phenotype, the age at onset of the epilepsy, the evolution of behavior and mental problems and the refractory nature of the epilepsy.

CASE REPORT :

The patient is a 2-year old girl, the third child of non-consanguineous parents, without familiar antecedents for epilepsy and/or mental retardation. She was born at 32 SA. Birth weight was 1080gr, size 40cm and head circumference (HC) 26 cm. She was referred to our department at the age of 2 years for seizures. Phenotypic examination revealed growth retardation, microcephaly (HC : 40,5 cm), facial dysmorphism, strabismus, eyelid anti-mongoloïd slots, and wide nasal bridge with bulbous tip, clears philtrum and micrognathia (Figure 1).

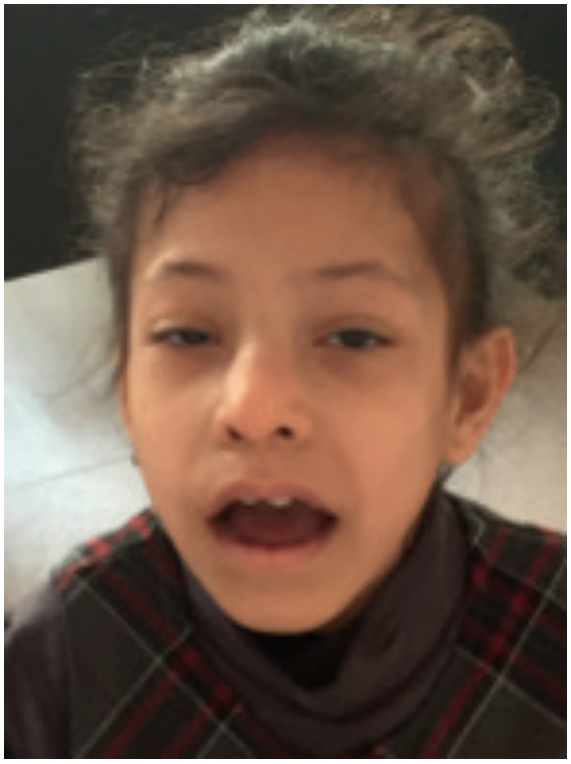

Figure 1 : Our patient at the age of 4 years

She had also single palmar crease and equine feet. Her psychomotor development was delayed: sitting at 18 months, unearned standing with a monosyllabic language.
First seizures began at the age of 2 years with prolonged absences, but within a month, she developed also generalized tonic-clonic seizures.
The ictal EEG during an absence showed a diffuse low voltage with long beats of rhythmic synchronous high-voltage with spike component predominantly in the frontal area. The inter-ictal EEG showed a bifrontal theta-delta activity suggesting a ring chromosome 20 syndrome (Figure 2)

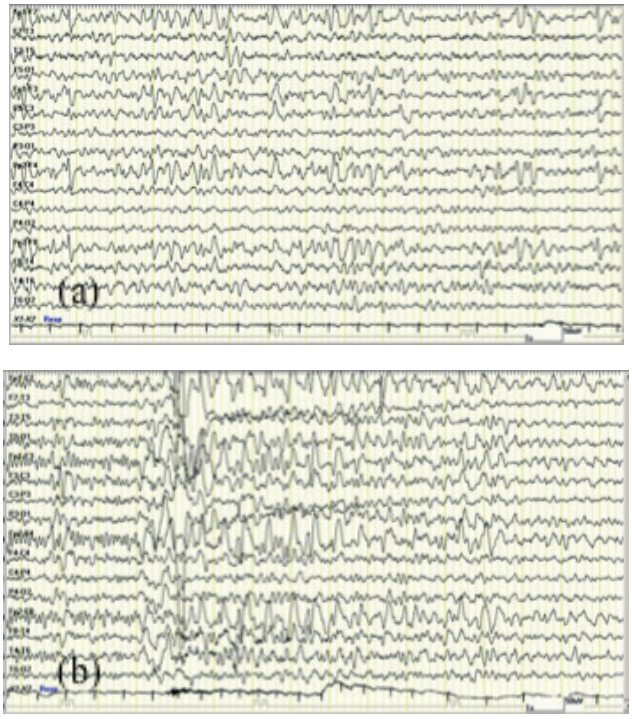

Figure 2 : (a): The inter-ictal EEG showing a bifrontal theta-delta activity. **(b):** The ictal EEG during an absence showing diffuse low voltage with long beats of rhythmic synchronous high-voltage with spike component predominantly in the frontal area.

which was confirmed by the karyotype (Figure 3).

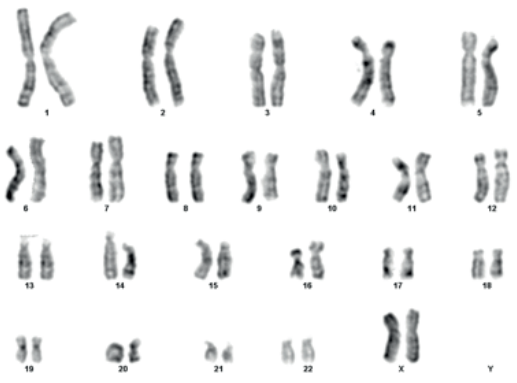

Figure 3 : karyotype of the patient illustrating the r(20)

Cranial MRI showed a diffuse cortical and subcortical atrophy.
The patient was initially treated with valproic acid witch reduced temporarily the frequency of the seizures but within 6 months we had to associate Levetiracetam and clonazepam witch reduced the frequency of the seizures.
Actually, she is 8 years old. She have a microcephaly (head circumference: 42 cm) and a severe intellectual deficiency. She is mute and apathetic. She continue to have seizures such as absence and generalized tonico clonic at a frequency of one per month.

DISCUSSION :

Ring chromosome 20 or r(20) syndrome is a rare chromosomal disorder that was initially described in 1972 by Atkins et al. [1] and approximately more than 100 affected individuals have been reported in the literature to date [2].

Seizures typically starts between three and five years of age with progressive severity and concomitant cognitive decline and usually remain refractory to anti-epileptic medication [2].

Typically, the patient with r(20) suffer from complex partial seizures which progress to generalized tonic or tonic-clonic seizures and nocturnal frontal lobe seizure [1-2]. To this brief motor seizures, patients with r(20) chromosome may present non convulsive status epilepticus (SE), which consists of a prolonged, confusional state like the seizure described initially in our patient. This type of seizure is often associated with EEG changes in the form of long-lasting, high voltage slow waves with occasional spikes, usually frontal [3]. Other types of seizures include terror, associated with loss of consciousness, automatisms or tonic activity.

The pathophysiology of seizures remains unclear. Rearrangements of two epilepsy genes, CHRNA4 and KCNQ2, have been raised as the cause. In fact, for the formation of the ring chromosome, the two telomeric regions of the chromosome must fuse and this could lead to loss of genetic materiel [3].

Dysmorphic features like described in our patient, such as microcephaly, slanting eyes and high palate, are found in only a minority of patients, which might explain the frequent delay in the diagnosis of this rare chromosomal disorder.

Additionally, progressive cognitive delay and behavioral problems are described [3-4].

Our patient suffered from mutism and apathy which was previously reported and that can be explained by the dysfunction of striatal dopamine in patients with r(20) [4].

Management of children with r (20) is symptomatic. A combination of valproate and lamotrigine is reportedly useful for treating non convulsive SE and improving the cognition [3,5].

CONCLUSION :

The ring chromosome 20 syndrome is characterized by childhood-onset refractory epilepsy, mental disability, and behavioral disturbances which can originate before seizure onset. Inter ictal EEG may be helpful for the diagnosis from ages of 4 to 5 years when it show 1- to 2-Hz delta slow waves and spike-and-waves predominating in the frontal areas.

RÉFÉRENCES :

[1] Atkins L, Miller WL, Salam M. A ring 20 chromosome.J Med Genet 1972;9:377-380.

[2] Conlin LK, Kramer W, Hutchinson AL, Li X, Riethman H, Hakonarson H, et al. Molecular analysis of ring chromosome 20 syndrome reveals two distinct groups of patients. J Med Genet. 2011 Jan;48(1):1-9.

[3] Zou YS1, Van Dyke DL, Thorland EC et al. Mosaic ring 20 with no detectable deletion by FISH analysis: Characteristic seizure disorder and literature review; Am J Med Genet A 2006; 140:1696-1706

[4] Biraben A, Semah F, Ribeiro MJ, Douaud G, Remy P, Depaulis A. Pet evidence for a role of the basal ganglia in patients with ring chromosome 20 epilepsy. Neurology 2004;63:73-7.

[5] Vignoli A, Canevini MP, Darra F, La Selva L, Fiorini E, Piazzini A, et al. Ring chromosome 20 syndrome: A link between epilepsy onset and neuropsychological impairment in three children; Epilepsia 2009; 50:2420-2427